REMARKS

The issues outstanding the Office Action mailed August 31, 2007, are the Priority Claim, the Information Disclosure Statement, the Restriction/Election, and the rejections under the doctrine of obviousness-type double patenting and 35 U.S.C. §101 and §112, as well as the objections to the claims. Reconsideration of these issues, in view of the following discussion, is respectfully requested.

Foreign Priority

It appears that the International Bureau has not sent a copy of the German Priority Document. Applicants have requested a copy of the Priority Document and will furnish the same when it is received.

Information Disclosure Statement

The Office Action does not state why the Information Disclosure Statement is in "partial compliance" with 37 CFR §1.97. However, it is assumed that this is because the IB did not send copies of the references cited in the International Search Report. Copies of the three references crossed out on the form 1449 are provided herewith, along with an additional Form 1449 for the examiner's initials. It is submitted that such copies are not needed to be provided by the applicant, in a National Stage application.

Restriction/Election

The examiner is thanked for indicating the withdrawal of the Requirement for Restriction/Election.

Double Patenting

Claims 1, 2 and 13-20 have been rejected under the doctrine of obviousness-type double patenting over Claims 1, 2 and 9-16 of co-pending application 10/594,024. Reconsideration of this rejection is respectfully requested.

It appears that the basis for this rejection is the argument that the present claims encompass the compounds of the co-pending application. In fact, it is not seen that R^4 and R^3 in the co-pending application suggest a compound within the scope of present generic

definitions of $R^2$and R^3 of the present application. In such a situation where the co-pending claims do not render obvious the rejected claims, it is submitted that an obviousness-type double patenting cannot stand. See, for example, *In re Vogle,* 422 F.2d 438, 164 USPQ 619 (CCPA 1970). Reconsideration of this rejection is thus respectfully requested.

Rejection under 35 U.S.C. §101

Claim 9 -12 have been rejected under 35 U.S.C. §101 as a result of the alleged use of the phrase "use of a compound." See page 18 of the Office Action. In fact, Claims 9 through 12 do not use the phrase. This term is only seen in Claims 18 and 20, which have been reformatted for U.S. practice. Withdrawal of the rejection is therefore respectfully requested.

Rejections under 35 U.S.C. §112, first paragraph

Claims 1-20 have been rejected under 35 U.S.C. §112, first paragraph, as a result of the recitation of the term "derivatives" in the claims. Reformatting of the claims for U.S. practice has eliminated this term, and withdrawal of this rejection is respectfully requested.

Claims 14, 15, 18 and 20 have been rejected under 35 U.S.C. §112, first paragraph, as argued to be non-enabled.

The thrust of this rejection, for example at page 12, appears to be recitation in the claims of the treatment of cancer. On the one hand, this rejection clearly does not appliy to Claim 20. Moreover, with respect to the claims which are directed to the treatment of tumor diseases, it is submitted that such utilities is clearly enabled by the specification. For example, the present specification at page 5, lines 4-16, indicates that the compounds of the invention inhibit factor VIIa. It is well known in the art that there is a correlation between tissue factor TF/factor VIIa and the development of various types of cancer, see, e.g., T. Taniguchi and N.R. Lemoine in Biomed. Health Res. (2000), 41 Molecular Pathogenesis of Pancreatic Cancer), 55-59. The publications listed below describe an antitumoral action of TF-VII and factor Xa inhibitors in various types of tumors:

K.M. Donnelly et al. in Thromb. Haemost. 1998; 79: 1041-1047;

E.G. Fischer et al. in J. Clin. Invest. 104: 1213-1221 (1999);

B.M. Mueller et al. in J. Clin. Invest. 101: 1372-1378 (1998); and

M.E. Bromberg et al. in Thromb. Haemost, 1999; 82: 88-92.

Moreover, on page 34 of the specification, Table 1 discloses two compounds presently claimed; with IC_{50} values for inhibiting factor TF/FVIIa. This clearly provides evidence that the present compounds are useful for these utilities. Consequently, the discussion in the specification, e.g., at page 5, lines 4-16, *without more* is sufficient to establish utility of the application for purposes of §112 of the statute, as it constitutes a scientifically supportable statement of utility which would be plausible to one of ordinary skill in the art.

It is well established that an unsupported suggestion that reactants within a class defined by claims in a typical method of use application would not work, or that such claims embrace inoperative members, is insufficient basis alone for rejecting the claims. See *Ex parte Janin*, 209 U.S.P.Q. 761 (POBA 1979). In fact, it is clear that recitations in an Applicants' specification *must* be taken by the PTO as an assertion that all compounds encompassed in the claims are operative in the invention, in the absence of reasons or evidence to the contrary. *In re Marzocchi*, 439 F.2d 220, 169 U.S.P.Q. 367 (CCPA 1971).

The first paragraph of 35 U.S.C §112 requires only *objective* enablement. Where a specification teaches the manner and process of making and using the invention, the specification *must* be taken as sufficient under §112, unless there is reason to doubt the truth of these statements. See *Marzocchi*, supra. Applicants' specification clearly enables one to make and use the disclosed compounds in the claimed methods, as evidenced from the disclosure at page 23-25 setting forth pharmaceutical formulations and dosages and the examples which also detail the production of a pharmaceutical formulations.

On the one hand, it is submitted that the Examiner has not provided any such reasons or evidence to doubt the assertion of utility in the specification and, thus, the further steps of the analysis as set forth in *Marzocchi* are not reached. Neither the alleged unpredictability in the art, nor the breadth of the claims, rise to the level of such reasons or evidence. As clearly stated in *Marzocchi*, mere *breadth* of the claims does not, without more, result in non-enablement. As the court stated in *Marzocchi*, supra

> Turning specifically to the objections noted by the Board as indicated above, it appears that these comments indicate nothing more than a concern over the *breadth* of the disputed term. If we are correct, then the relevance of this concern escapes us. It has never been contended that

> Applicants, when they included the disputed terms in their specification, intended only to indicate a single compound. Accepting, therefore, that the term is a generic one, its recitation must be taken as an assertion by Applicants that all of the 'considerable number of compounds' which are included in the generic term would, as a class, be operative to produce the asserted enhancement of adhesion characteristics. The only relevant concern of the patent office under these circumstances should be over the *truth* of any such assertion. The first paragraph of §112 requires nothing more than *objective enablement*. How such a teaching is set forth, either by the use of illustrative examples or by broad term analogy, it is of no importance.

Marzocchi, supra (Emphasis in original). Thus, the concern expressed at pages 3 and 7 of the Office Action, apparently that many types of cancers are encompassed in the claimed methods, does not provide the reasons or evidence necessary by *Marzocchi* to pass beyond the necessity for objective enablement.

Further, in this regard, it is important to note, as a matter of law, that it is not necessary for Applicants' *method* claims to exclude inoperative embodiments, inasmuch as the claims are interpreted in light of the level of understanding one of ordinary skill in the art and, for methods, are interpreted to be *per se* functional. See *In re Angst*, 190 U.S.P.Q. 214 (CCPA 1976) and *In re Dinh-Nguyen*, 181 U.S.P.Q. 46 (CCPA 1974). These cases state that, for method claims, inoperative embodiments are not encompassed therein and the only questions is whether it would be undue experimentation for one of ordinary skill in the art to determine the scope of the claim. This issue is discussed more fully below. Moreover, anti-tumor utilities are no longer to be considered to be "special", i.e., per se incredulous, by the Patent and Trademark Office. See *Ex parte Rubin*, 5. USPQ 2d 1461 (BPAI 1987). As such, applications claiming these methods are, therefore, no more than typical method of use applications wherein the existence of reliable screening protocols correlatable with pharmaceutical activity in humans is sufficient to satisfy §112, in the absence of reasons to the contrary. As noted above, screening protocols for determining the effacy of the compounds in the anti-tumor utilities are set forth in the specification where it is indicated that the details of using a given compound can be determined by routine testing using a known protocol which is correlated with human activity, again, see page 3, lines 18-31 and page 3, lines 30-34.

Thus, the only way that the issue of "undue experimentation" comes up is if the PTO were to furnish reasons or evidence why the objective enablement of the present specification fails (none have been advanced) or it is alleged it would have been undue experimentation to determine the *scope* of the present method claims. Thus, the discussion of *In re Wands*, taking up a substantial amount of the Office Action, does *not* provide the necessary reasons or evidence as to why utility is deficient, but instead is reached only in other circumstances, e.g., to assess "undue experimentation," *only* once reasons or evidence to doubt objective enablement are established. However, since this analysis has been given considerable breadth in the Office Action, it will be addressed herein.

With respect to the nature of the invention, the *unpredictability* is in fact not supported by the breadth of the claim, as apparently argued, for example, at page 13. In actuality, the nature of the invention is not unpredictable, inasmuch as the use of VIIa inhibitors to treat tumors is well established and would be well understood by one of skill in the art.

With respect to the breadth of the claims, it is important to note that a determination of undue experimentation must be considered on a *compound by compound* or *indication by indication* basis. The mere fact that a claim is broad does *not* mean that it is undue experimentation is required to determine enablement of the compounds therein, if it is not undue experimentation to determine enablement for *each* compound or indication in the scope of the claim. See, for example, *In re Colianni*, 195 U.S.P.Q. 150 (CCPA 1977). One of ordinary skill in the art can easily determine whether a given compound has the utility stated against a given cancer. Thus, the mere fact that many compounds or tumor types must be tested is not dispositive of lack of utility.

With respect to the guidance given by the instant specification, is submitted that the guidance is adequate, inasmuch as pharmaceutical formulation information is given, one of ordinary skill in the art can clearly prepare the compounds for administration, dosages are given and the pharmaceutical art is well developed and administration of a compound for a given indication is quite routine. The discussion at page 13 of the Office Action appears to be speculation on the part of the PTO that mechanisms are not well understood, however, elucidation of a mechanism is *not* necessary, where sufficient instruction is given to administer the compounds to produce the desired effect. Thus, it is submitted that this is also a non-issue.

With respect to working examples, it is well established that working examples are *not*

required to provide enablement. See, for example, *In re Borkowski*, cite.

With respect to the state of the art, factor VIIa inhibitors are well known to be implicated in signaling pathways which are instrumental in the formation of tumors. Thus, it is again not seen that this is an issue. With respect to the quantity of invention necessary, this has been discussed above. It is maintained that the fact that a claim may be broad does not, in and of itself, result in undue experimentation, if the testing of, for example, each type of cancer is routine. Thus, this is not seen to be basis for lack of enablement.

In conclusion, it is submitted that the Wands factors clearly support undue experimentation in order to determine whether a given cancer and/or autoimmune disease indication and/or a compound is within the scope of the present claims. Thus, objective enablement is clearly present, and withdrawal of the rejection under 35 U.S.C §112 is respectfully requested.

Rejections under 35 U.S.C. §112, second paragraph

Claims 1-20 have also been rejected under 35 U.S.C. §112, second paragraph. Reformulation of these claims for U.S. practice obviates these rejections, and withdrawal thereof is respectfully requested.

Claims 18 and 20 have also been rejected under 35 U.S.C. §112, second paragraph. Again, reformulation of these claims also obviates this rejections, and withdrawal thereof is respectfully requested.

Additionally, Claims 17, 19 and 20 have been rejected under 35 U.S.C. §112, second paragraph. It is respectfully submitted that the term "at least one further medicament active ingredient" is clearly defined in the specification, for example, at page 6, as noted in the Office Action. It is not seen that one of ordinary skill in the art would find this claim to be indefinite, and withdrawal of this rejection is therefore respectfully requested.

Finally, Claim 13 has been rejected under 35 U.S.C. §112, second paragraph. Again, reformulation of this claim for U.S. practice obviates this rejection, and withdrawal thereof is respectfully requested.

The claims in the application are submitted to be in condition for allowance. However, if the examiner has any questions or comments, he or she is cordially invited to telephone the undersigned at the number below.

No fee is believed due with this response, however, the Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

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